

**Faculty of Health**

**Centre for Cardiovascular and Chronic Care**

**Renal function in chronic heart failure: a cohort study**

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**This thesis is presented for the Degree of**

**Doctor of Philosophy**

**University of Technology, Sydney**

**8<sup>th</sup> December 2014**

## Acknowledgement

“...You ought to know how to discern among incoherent and varying ideas and systems that which is true or fruitful in each. ...In this patient search for truth and a habit of fairness that we ought to have toward others and their ideas, we need integrity of mind, clear judgment, and solid learning. You will gradually acquire these things, and you will do so more easily when your convictions become more consciously developed...” (Elisabeth Leseur died 1914). These thoughts expressed by Elisabeth Leseur, a French married laywoman whose cause for canonisation is underway, not only reflect the spiritual life; life in general but are particularly pertinent to the PhD process. One realises it is only by God’s grace, *‘I can do all things in Him who strengthens me’ (Phil 4:12-14)*.

Grace has come to me via the strong support of my supervisors, family, peer group and friends. My principal supervisor Dr Patricia Davidson now the Dean of Nursing at Johns Hopkins University has stayed the journey with me despite all the challenges she has faced in taking up her role at JHU. Trish encouraged me, guided me and didn’t give up on me during some very stressful times. Dr Phillip Newton my co-supervisor has also been a pillar of support. His generous, calm, good nature was the ideal foil to my sometimes frayed persona, especially when the statistical challenge was getting the better of me. To Dr Chakra Budhathoki, Johns Hopkins University and Dr David Sibbritt at the University of Technology (UTS) I am truly grateful for the statistical insights and direction. One of the most helpful people at the very beginning of this journey was Ms Jane Van Balen, a senior librarian at UTS. Jane was very generous with her time and especially good-natured in responding to my many questions when guiding me in developing the literature review strategy.

The collaboration of the study site co-investigators Professor Dominic Leung, Dr Stephen Spicer and nurse Kay Johnson are gratefully acknowledged - without their support there would have been no access to the study cohort. Their contribution to the published article and feedback

for the peer review process was great when encouragement was needed. To Nisveta, Elizabeth, and Lilly from the clinical information centre at the study site a great deal of gratitude is in order. These 3 wonderful people were involved in generating the cohort and in collecting case records need for the study. Thank you.

The opportunity to study for a PhD is a family affair. Without the love and selflessness of my partner Kay, I would not be at this stage of submitting my PhD Thesis. She has given her love, her silence (wearing headphones to watch TV!), service in cooking meals, exercising the dogs, mowing the lawns and all the other things that you have to do to keep life ticking over so I could study. Kay, I love you very much and I am incredibly grateful to you. Family is also very much about mum, dad, and siblings. Although they did not have a great understanding of what this PhD has been all about, they have never stopped supporting me with their love and prayers. I know many graces and blessing have come to me through them, Joyce my wonderful stepmum, Jan, Caryl, John and Ian. Noel my dad who passed away many years ago always prayed for me and with my natural mum, Doreen who also died a long time ago I know they have had direct access with their prayer!

I thank and dedicate my thesis to all those study participants who have over the years, by their willingness to participate in medical research, made the greatest contribution to improving the health and well-being of their brothers and sisters; and to all who have enabled me to come to this place in my life.

*NON NOBIS DOMINE, SE NOMINI TUO DA GLORIAM*

Psalm 115:1

## **Anthology of publications and presentations associated with this thesis**

### **Papers Published**

Sheerin NJ, Newton PJ, Macdonald PS, Leung DY, Sibbritt D, Spicer ST, Johnson K, Krum H, Davidson PM. Worsening renal function in heart failure: the need for a consensus definition. *Int J Cardiol.* 2014 Jul 1; 174(3):484-91. doi: 10.1016/j.ijcard.2014.04.162. Epub 2014 Apr 21. PubMed PMID: 24801076. **(Impact factor 6.18)**

Deek H, Newton P, Sheerin N, Nouredine S, Davidson PM. Contrast media induced nephropathy: A literature review of the available evidence and recommendations for practice. *Aust Crit Care.* 2014 Jan 22. pii: S1036-7314(13)00266-X. doi: 10.1016/j.aucc.2013.12.002. [Epub ahead of print] PubMed PMID: 24461960. **(Impact factor 1.27)**

Shehab S, Luckett T, Phillips JL, Currow DC, Newton PJ, Thompson SC, Sheerin NJ, Allida SM, Di Salvo D, Inglis SC, Davidson PM. *(In preparation)* Chart reviews: an overlooked and important data source and recommendations for methodological standards.

### **Conferences/presentations**

Sheerin NJ, Newton PJ, Macdonald PS, Leung DY, Spicer ST, Johnson K, Krum H, Davidson PM. Would acute kidney injury definitional concordance across generalist & specialist health professional groups improve patient outcomes? Poster presentation at the Guidelines International Network (G-I-N) Conference, 20<sup>th</sup> to 23rd August, 2014. *Melbourne, Australia.*

## **Certificate of original authorship**

I certify that the work in this thesis has not previously been submitted for a degree nor has it been submitted as part of requirements for a degree except as fully acknowledged within the text.

I also certify that the thesis has been written by me. Any help that I have received in my research work and the preparation of the thesis itself has been acknowledged. In addition, I certify that all information sources and literature used are indicated in the thesis.

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Date:

8<sup>th</sup> December 2014

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## **Abstract**

Renal dysfunction is strongly associated with adverse health outcomes in chronic heart failure. The term cardio-renal syndrome has been proposed to describe the theoretical models developed to explain the pathophysiological mechanisms underpinning the condition and many observational studies undertaken to characterise and identify risk factors and morbidity and mortality outcomes. There is evidence baseline glomerular filtration rate is a stronger predictor of mortality in patients with Heart Failure than left ventricular ejection fraction or NYHA functional class. However, the ambiguity surrounding definitions and nomenclature for renal dysfunction in heart failure has impeded progress for a clearly defined risk profile and characterization for heart failure patients with renal impairment, chronic kidney disease, worsening renal function, or acute kidney injury. The focus of this study was to characterize an Australian cohort of hospitalised heart failure patient who developed acute kidney injury, and investigate this relationship in terms of morbidity and mortality at 12-months follow-up. A secondary purpose was to determine the prevalence of confirmed chronic kidney disease and renal impairment in the cohort and their outcomes. The results highlight the prevalence of Renal Insufficiency and Chronic Kidney Disease, 59% and 52% respectively. Acute kidney injury occurred in 1 in 4 patients when diagnosed using a modified AKIN definition. Characterization of HF patients with any type of renal abnormality revealed a history of multiple comorbidities where concurrent diabetes exposed hospitalised HF patients to an increased risk of AKI. From an original sample of 265 admissions, 166 had data available for the 12-month follow-up morbidity and survival analysis. The reduced sample size limited the study power, such that only renal impairment was trending towards significance. The Kaplan-Meier survival distributions for acute kidney injury and renal impairment at 12-months follow-up was not statistically significant, log-rank  $p=0.4714$  and  $p=0.0579$  respectively. The findings confirm the high incidence and prevalence of renal dysfunction in hospitalised heart failure patients and demonstrate the utility of the AKIN AKI definition. The study strengthens the call for

community monitoring of renal function and the need for definitional and nomenclature consensus. A move towards improved monitoring and a standardised taxonomy would assist with differentiating renal dysfunction types and may lead to better risk stratification of HF patients for adverse events.

## Abbreviations

Abbreviation	Full term
ABS	Australian Bureau of Statistics
ACCF	American College of Cardiology Foundation
ACE	Angiotensin-converting enzyme
ACE -I	Angiotensin-converting enzyme - Inhibitor
ACR	Albumin Creatinine Ratio
ADHF	Acute Decompensated Heart Failure
AHA	American Heart Association
AKI	Acute Kidney Injury
AKIN	Acute Kidney Injury Network
ARB	Angiotensin II Receptor Blocker
BiPAP	Biphasic intermittent positive airway pressure
BMI	Body mass index
BSA	Body surface area
CAD	Coronary artery disease
CGE	Cockcroft-Gault Equation
CHF	Chronic Heart Failure or Congestive Heart Failure
CI	Confidence interval
CKD	Chronic Kidney Disease
CKD-EPI	Chronic Kidney Disease Epidemiology Collaboration
CKMB	Creatine kinase myocardial band isoenzyme
COPD	Chronic obstructive pulmonary disease

<b>Abbreviation</b>	<b>Full term</b>
CPAP	Continuous positive airway pressure
CPGs	Clinical practice guidelines
CrCl	Creatinine clearance
CRF	Clinical or case report form
CRS	Cardiorenal syndrome
CVD	Cerebrovascular disease
DBP	Diastolic blood pressure
ECS	European Society of Cardiology
ED	Emergency Department
eGFR	Estimated Glomerular Filtration Rate
EPR	Electronic patient record
GFR	Glomerular Filtration Rate
GTN	Glyceryl Trinitrate
HREC	Human Research Ethics Committee
HF	Heart Failure
HFpEF	Heart Failure preserved ejection fraction
HFrEF	Heart failure reduced ejection fraction
HHF	Hospitalised heart failure
HR	Hazard Ratio
hrs	Hours
ICD-10-AM Codes	International Classification of Diseases 10 <sup>th</sup> revision Australian Modification based on the World Health Organization's internationally accepted classification of death and disease
ICU	Intensive Care Unit

<b>Abbreviation</b>	<b>Full term</b>
IQR	Inter quartile range
IV	Intravenous
IVI	Intravenous infusion
JVP	Jugular venous pressure
KDIGO	Kidney Disease Improving Global Outcomes
KDOQI	Kidney Disease Outcomes Quality Initiative
KIM-1	Kidney injury molecule-1
LOS	Length of stay
LVF	Left ventricular function
MACE	Major acute cardiac event
MCV	Mean cell volume
MDRD	Modification of Diet in Renal Disease
MRAs	Mineralocorticoid receptor antagonists
NGAL	neutrophil gelatinase-associated lipocalin
NKF	National Kidney Foundation
Non-STEMI	Non S-T Elevation Myocardial Infarct
NSAIDs	Non-steroidal anti-inflammatory drugs
NYHA	New York Heart Association
OR	Odds Ratio
RCT	Randomised Control Trials
RD	Renal dysfunction
RDW	Red cell distribution width
ReFinH	Renal function in heart failure study

<b>Abbreviation</b>	<b>Full term</b>
RI	Renal Impairment/ Insufficiency
RIFLE	Risk-Injury-Failure-Loss-Endstage renal disease
RR	Relative Risk
SaO2	Arterial oxygen saturation
SBP	Systolic blood pressure
SCr	Serum creatinine
SD	Standard deviation
SIEFA	Socio-economic Indexes for Areas
sMDRD	Simplified Modification of Diet in Renal Disease
SPSS	Statistical Package for Social Sciences
STEMI	S-T Elevation Myocardial Infarct
SWSLHN	South Western Sydney Local Health Network
UTS	University of Technology
VAD	Ventricle assist device
WRF	Worsening Renal Function

## Glossary

Terms	Definition
Acute heart failure	De novo acute heart failure or decompensated chronic heart failure characterized by signs of pulmonary congestion, including pulmonary oedema
Acute kidney injury	AKI is a syndrome characterised by the <i>rapid</i> loss of the kidney's excretory function which is typically diagnosed by an significant increase in serum creatinine
Body mass index	A measure of an adult's weight (body mass) relative to height used to assess the extent of weight deficit or excess. BMI uses a simple calculation based on the ratio of someone's height and weight ( $\text{BMI} = \text{kg/m}^2$ ).
Cardiovascular disease	A disease affecting the heart or blood vessels. Cardiovascular diseases include arteriosclerosis, coronary artery disease, heart valve disease, arrhythmia, heart failure, hypertension, orthostatic hypotension, shock, endocarditis, diseases of the aorta and its branches, disorders of the peripheral vascular system, and congenital heart disease
Chronic condition	A health condition that is long term; has a pattern of recurrence, or deterioration; has a poor prognosis and produces consequences, or sequelae that impact on the individual's quality of life
Chronic heart failure	A complex clinical syndrome with typical symptoms (e.g. shortness of breath, fatigue) that can occur at rest or on effort, and is characterised by objective evidence of an underlying structural abnormality of cardiac dysfunction that impairs the ability of the ventricle to fill with or eject blood (particularly during physical activity).
Chronic kidney disease	Abnormalities of kidney structure or function, present for more than 3 months, with implications for health and classified based on cause, GFR category, and albuminuria category
Comorbidity	When a person has two or more health problems at the same

Terms	Definition
	time
Confidence interval (CI)	A statistical term describing a range (interval) of values within which we can be 'confident' that the true value lies, usually because it has a 95% or higher chance of doing so
Diabetes	A disease marked by high blood glucose levels resulting from defective insulin production, insulin action or both. The three main types of diabetes are type-1 diabetes, type-2 diabetes and gestational diabetes. Where a person has a history of diabetes; a diagnosis of diabetes.
Dyspnoea	Difficult or laboured breathing; shortness of breath
Ejection fraction	Refers to the amount, or percentage, of blood that is pumped out of the ventricles with each contraction; the left ventricle percentage is most frequently recorded
Health outcome	A change in the health of an individual, or a group of people or a population, which is wholly or partially attributable to an intervention or a series of interventions
Heart failure	Described in physiological terms HF is a syndrome characterized by either or both pulmonary and systemic venous congestion and/or inadequate peripheral oxygen delivery, at rest or during stress, caused by cardiac dysfunction.
Incidence	Refers to the number of individuals who develop a specific disease or experience a specific health-related event during a particular time period (such as a month or year)
Length of stay	Duration of hospital stay, calculated by subtracting the date the patient is admitted from the day of separation. A same-day patient is allocated a length of stay of 1 day
Local hospital network	LHNs are small groups of local hospitals, or an individual hospital, linking services within a region or through specialist networks across a state or territory.
Morbidity	Refers to ill health in an individual and to levels of ill health in



Terms	Definition
	a population or group
New York Heart Association – functional class	Mainly describes the functional limitations of the patient such that <u>Class I</u> – ordinary physical activity does not cause undue fatigue, palpitations, dyspnoea and/or angina; <u>Class II</u> - ordinary physical activity does cause undue fatigue, palpitations, dyspnoea and/or angina; <u>Class – III</u> Less than ordinary physical activity cause undue fatigue, palpitations, dyspnoea and/or angina; and <u>Class- IV</u> fatigue, palpitations, dyspnoea and/or angina occur at rest.
Orthopnoea	Discomfort or difficulty breathing when lying flat
Prevalence	Refers to the total number of individuals in a population who have a disease or health condition at a specific period of time, usually expressed as a percentage of the population
Principal diagnosis	The diagnosis listed in hospital records to describe the problem that was chiefly responsible for the patient’s episode of care in hospital
Quality of life	A generic term that measures the individual’s perception of their life experience. It is a multidimensional concept measuring important aspects or domains of a person’s life including physical functioning, psychological processes and social and economic concerns, as well as spiritual and existential aspects.
Renal impairment	Acute or chronic kidney failure also known as ‘renal insufficiency’ or ‘renal dysfunction’ It is a medical condition in which the kidneys fail to adequately filter waste products from the blood.
Risk Factors	A risk factor is any attribute, characteristic or exposure of an individual that increases the likelihood of developing a disease or injury
Stroke	Diagnosis for ischaemic: non-haemorrhagic cerebral infarction or haemorrhagic: intracerebral haemorrhage supported by

Terms	Definition
	cerebral imaging
Taxonomy	A classification containing domains and subcategories for the measurement properties and aspects of measurement properties which are the subcategories
Albuminuria	An abnormal excretion rate of albumin (protein) in the urine
Glomerular filtration rate	The amount of ultrafiltrate formed by plasma flowing through the glomeruli of the kidney.